AMENDMENT TO THE CLAIMS

1. **(Currently Amended)** An adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being a cotranslational fusion protein encoded by a recombinant nucleic acid, and comprising a protease domain that catalyzes the proteolytic cleavage of at least one peptide bond of the substrate polypeptide so as to inhibit the activity of the polypeptide, and a targeting domain that reversibly binds with an address site on said substrate polypeptide, wherein said targeting domain and said protease domain are discrete and heterologous with respect to each other, and wherein said adzyme is resistant to cleavage by said protease domain.

2. **(Canceled)**

3. **(Withdrawn)** The adzyme of claim 1, wherein said protease domain is a zymogen.

4. **(Original)** The adzyme of claim 1, wherein said protease domain is selected from among: a serine proteinase and a metalloproteinase.

5. **(Original)** The adzyme of claim 1, wherein said adzyme is purified from a cell culture in the presence of a reversible protease inhibitor that inhibits the protease activity of the protease domain.

6-13. **(Canceled)**

14. **(Previously Presented)** The adzyme of claim 1, wherein said targeting domain and said protease domain are joined by a linker comprising an unstructured peptide.

15. **(Currently Amended)** The adzyme of claim 14, wherein said linker includes one or more repeats of Ser_4Gly (SEQ ID NO: 7) or $SerGly_4$ (SEQ ID NO: 8) or Gly_4Ser (SEQ ID NO: 17).

16. **(Previously Presented)** The adzyme of claim 14, wherein said linker is selected to provide steric geometry between said protease domain and said targeting domain such that said adzyme is more active than said protease domain or targeting moiety with respect to the reaction with said substrate.

17. **(Previously Presented)** The adzyme of claim 14, wherein said linker is selected to provide steric geometry between said protease domain and said targeting moiety such that said address moiety presents the substrate to the enzymatic domain at an effective concentration at least 5 fold greater than would be present in the absence of the address moiety.

18. **(Canceled)**

19. **(Previously Presented)** The adzyme of claim 1, wherein the substrate polypeptide is an extracellular polypeptide, and wherein said activity is receptor-mediated signaling activity.

20. **(Previously Presented)** The adzyme of claim 1, wherein the adzyme is resistant to autocatalyzed proteolysis at an adzyme concentration that is about equal to the concentration of adzyme in a solution to be administered to a subject.

21. **(Previously Presented)** The adzyme of claim 1, wherein said substrate is present in biological fluid of an animal.

22. **(Original)** The adzyme of claim 21, wherein said biological fluid is blood or lymph.

23. **(Original)** The adzyme of claim 21, wherein said substrate is a polypeptide hormone, a growth factor and/or a cytokine.

24. **(Original)** The adzyme of claim 21, wherein said substrate is selected from among: four-helix bundle factors, EGF-like factors, insulin-like factors, β-trefoil factors and cysteine knot factors.

25. **(Original)** The adzyme of claim 21, wherein said substrate is an inflammatory cytokine and said enzyme construct reduces the pro-inflammatory activity of said polypeptide factor.

26. **(Original)** The adzyme of claim 1, wherein the targeting domain is an antibody or polypeptide(s) including an antigen binding site thereof.

27. **(Original)** The adzyme of claim 1, wherein the targeting moiety is selected from the group consisting of a monoclonal antibody, an Fab and $F(ab)_2$, an scFv, a heavy chain variable region and a light chain variable region.

28. **(Withdrawn)** The adzyme of claim 1, wherein said substrate is a receptor ligand, and said targeting domain includes a ligand binding domain of a cognate receptor of said ligand.

29. **(Withdrawn)** The adzyme of claim 1, wherein said targeting domain is an artificial protein or peptide sequence engineered to bind to said substrate.

30. **(Original)** The adzyme of claim 1, wherein the substrate is endogenous to a human patient.

31. **(Previously Presented)** The adzyme of claim 30, wherein the effect of the adzyme on the substrate is not significantly affected by the presence of a human serum protein when tested with a concentration of the substrate that is about 0.5 to 2 times the expected physiological concentration of substrate and a concentration of the human serum protein that is about 0.5 to 2 times the expected physiological concentration of the human serum protein.

32. **(Previously Presented)** The adzyme of claim 31, wherein the human serum protein is human serum albumin.

33. **(Original)** The adzyme of claim 1, wherein said adzyme alters the half-life of the substrate *in vivo*.

34. **(Original)** The adzyme of claim 1, which alters an interaction between the substrate and a receptor.

35-36. **(Canceled)**

37. **(Original)** A pharmaceutical preparation comprising the adzyme of claim 1 and a pharmaceutically effective carrier.

38. **(Original)** The pharmaceutical preparation of claim 37, formulated such that autocatalytic proteolysis of the adzyme is inhibited.

39. **(Original)** The pharmaceutical preparation of claim 38, further comprising a reversible inhibitor of said protease domain.

40. **(Original)** The pharmaceutical preparation of claim 39, wherein the reversible inhibitor is safe for administration to a human patient.

41. **(Previously Presented)** An adzyme for inhibiting an activity of a substrate polypeptide, the adzyme being an immunoglobulin fusion complex comprising: a first fusion protein bound to a second fusion protein, wherein the first fusion protein comprises a constant portion of an immunoglobulin heavy chain and a protease domain that catalyzes the proteolytic cleavage of at least one peptide bond of the substrate polypeptide so as to inhibit the activity of the polypeptide, and wherein the second fusion protein comprises a constant portion of an immunoglobulin heavy chain and a targeting domain that reversibly binds with an address site on said substrate polypeptide, wherein said targeting domain and said protease domain are discrete and heterologous with respect to each other, and wherein said adzyme is resistant to cleavage by said protease domain.